

Abstract

Isolated ligands which bind a molecule expressed on the surface of T cells and induce
5 antigen specific apoptosis in activated T cells are disclosed. Preferably, the T cell surface
molecule is CTLA4 and the ligand is a monoclonal anti-CTLA4 antibody that binds to an
epitope of CTLA4 distinct from the binding sites of B7-1 and B7-2. Upon binding of the
antibody to CTLA4 on an activated T cell, in the presence of an antigenic signal, antigen
specific apoptosis is induced. The invention also describes a novel natural CTLA4 ligand,
10 distinct from B7-1 and B7-2, which mediates induction of apoptosis. Pharmaceutical
compositions of anti-CTLA4 antibodies or other isolated CTLA4 ligands which can be
administered to subjects to induce T cell apoptosis, thereby clonally deleting antigen specific
T cells, such as alloreactive T cells in transplantation situations or autoreactive T cells in
autoimmune disorders, are also disclosed. Methods for inducing T cell apoptosis *in vitro*
15 with an anti-CTLA4 antibody or other ligand of the invention together with an antigen
specific signal are also disclosed, *e.g.*, for use in purging alloreactive T cells from donor bone
marrow prior to bone marrow transplantation to inhibit graft versus host disease.